

REMARKS/ARGUMENTS

This is meant to be a complete response to the Office Action mailed May 10, 2005. In the Office Action, the Examiner rejected Applicants' claims 1, 3, 6, 7, 10, 13, 24, 25, 27, 44, 45 and 47 under 35 U.S.C. 112, ¶1, as failing to comply with the written description requirement, and under 35 U.S.C. 112, ¶2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner rejected claims 1, 7, 10, 13 and 24-25 under 35 U.S.C. 102(b) as being anticipated by Badylak et al. (US 5,695,998); claims 1, 3, 6, 7, 10, 13, 24, 25 and 27 under 35 U.S.C. 103(a) as being unpatentable over Badylak et al. in view of the two Zhang et al. references (*Pediatrics Journal*, 1999 and *Journal of Urology*, 2000); and claims 44, 45, and 47 under 35 U.S.C. 103(a) as being unpatentable over Badylak et al. in view of the two Zhang et al. references.

Applicants' Response to the 35 U.S.C. 112, ¶1 Rejection

In the Office Action, the Examiner rejected Applicants' claims 1, 3, 6, 7, 10, 13, 24, 25, 27, 44, 45 and 47 under 35 U.S.C. 112, ¶1, as failing to comply with the written description requirement.

In support of the rejection, the Examiner stated that "there are many types of the generic 'stem' cells and applicant has failed to show possession of the entire scope of 'stem' cell".

Applicants respectfully traverse the rejection; however, for the sake of expediting issuance of a patent from the subject application, the term "stem cell" has been amended in currently pending claims 1, 6, 7, 10, 13, 24, 25, 44 and 45 to "bone marrow stromal cell". Support for the use of bone marrow stromal cells in the production of a urinary tract tissue graft composition for repairing a damaged urinary tract tissue can be found in Paragraphs [0022], [0024], [0058]-[0065] and [0071]-[0075] and Table I of the Specification, as well as in Figures 6-11 of the subject application.

Therefore, Applicants respectfully submit that claims 1, 6, 7, 10, 13, 24, 25, 44 and 45, as now pending, fully comply with the written description requirement of 35 U.S.C. 112, ¶1. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 112, ¶1 rejection of the claims as now pending.

Applicants' Response to the 35 U.S.C. 112, ¶2 Rejection

In the Office Action, the Examiner rejected Applicants' claims 1, 3, 6, 7, 10, 13, 24, 25, 27, 44, 45 and 47 under 35 U.S.C. 112, ¶2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In support of the rejection, the Examiner stated that:

It is unclear what applicant's actual invention is because it is unclear what actual "stem cells" are used in the invention or what

the actual cells of the graft are when they are used for repair. Applicant's claims don't require differentiation however many of they claims require "maturation" and "penetrance" which would appear to involve differentiation.

In response to the rejection, currently pending claims 1, 6, 7, 10, 13, 24, 25, 44 and 45 have been amended herein to claim "bone marrow stromal cells" instead of "stem cells", as discussed herein previously, and the independent claims 1, 24 and 44 have been amended herein to recite that the "bone marrow stromal cell differentiates into a smooth muscle-like cell".

Therefore, Applicants respectfully submit that claims 1, 6, 7, 10, 13, 24, 25, 44 and 45, as now pending, are definite and particularly point out and distinctly claim that which Applicants regard as the invention. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 112, ¶2 rejection of the pending claims.

Applicants' Response to the 35 U.S.C. 102(b) Rejection

In the Office Action, the Examiner rejected claims 1, 7, 10, 13 and 24-25 under 35 U.S.C. 102(b) as being anticipated by Badylak et al. (US 5,695,998). Applicants respectfully traverse the rejection based on the amendments to the claims and for the reasons stated hereinbelow.

The claims of the subject application, as now pending, recite a urinary tract tissue graft composition and a method for providing the same, as well as

a method for repairing a damaged urinary tract tissue of a subject. The urinary tract tissue graft composition includes a segment of small intestinal submucosa and at least one **bone marrow stromal cell** seeded thereon, wherein the bone marrow stromal cell **differentiates into a smooth muscle-like cell** and exhibits three dimensional growth and matrix penetrance.

Badylak et al. teach a cell culture growth substrate comprising submucosal tissue and eukaryotic cells contacted thereto. Badylak et al. teach growing a variety of **unipotent** cell types on submucosal tissue. While Badylak et al. briefly mention seeding mesenchymal cells on the submucosal tissue at Column 6, lines 34-36, Badylak et al. simply teach **expansion** of this cell population on the submucosal tissue and NOT differentiation of the mesenchymal cells into another cell type on the submucosal tissue. Further, Badylak et al. simply suggest that mesenchymal cells could be seeded on submucosal tissue, but Badylak et al. do not demonstrate that mesenchymal cells will actually grow on submucosal tissue, and therefore Badylak et al. do not enable a teaching of seeding mesenchymal cells on submucosal tissue.

In addition, the only other reference in Badylak et al. to differentiation is found in Example 5. However, the "cytodifferentiation" of Example 5 refers to **unipotent**, fetal epithelial cells differentiating into adult epithelial cells by the natural epithelial cell maturation process. This is not the same as, nor similar to, the differentiation of a multipotent cell into a different cell type. Badylak et

al. do not teach, disclose or even suggest differentiation of a multipotent cell into a different cell type on submucosal tissue, as Badylak et al. only teach expansion, maturation and proliferation of unipotent cells on submucosal tissue. Thus, Badylak et al. do not enable a cell culture growth substrate comprising submucosa and stem cells, as the Examiner has asserted. The presently claimed invention is the **first** demonstration of differentiation of a multipotent cell into another cell type on submucosal tissue.

In addition, Badylak et al. do not teach, disclose or even suggest growing urinary tract cells on submucosal tissue, nor do Badylak et al. teach, disclose or even suggest methods of providing a urinary tract tissue graft composition or repairing a damaged urinary tract tissue, nor do Badylak et al. teach seeding a multipotent cell on submucosal tissue such that the multipotent cell differentiates into a urinary tract cell type.

Therefore, Applicants respectfully submit that amended claims 1, 7, 10, 13 and 24-25 are not anticipated by Badylak et al. (US 5,695,998). Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 102(b) rejection of the claims as now pending.

Applicants' Response to the 35 U.S.C. 103(a) Rejections

In the Office Action, the Examiner rejected claims 1, 3, 6, 7, 10, 13, 24, 25 and 27 under 35 U.S.C. 103(a) as being unpatentable over Badylak et al. in

view of the two Zhang et al. references (*Pediatrics Journal*, 1999 and *Journal of Urology*, 2000), and also rejected claims 44, 45, and 47 under 35 U.S.C. 103(a) as being unpatentable over Badylak et al. in view of the two Zhang et al. references. Applicants respectfully traverse the rejections based on the amendments to the claims, for the reasons stated above in response to the 35 U.S.C. 102(b) rejection of the claims over Badylak et al., and for the reasons stated hereinbelow.

As stated hereinabove in response to the 35 U.S.C. 102(b) rejection of the claims as anticipated by Badylak et al., Badylak et al. do not teach, disclose or even suggest a urinary tract tissue graft composition and methods for providing and using tje same, wherein the urinary tract tissue graft composition includes a segment of small intestinal submucosa and at least one **bone marrow stromal cell** seeded thereon, wherein the bone marrow stromal cell differentiates into a smooth muscle-like cell.

The Examiner has recognized the deficiencies of Badylak et al. and has attempted to supply such deficiencies with the teachings of the two Zhang et al. references. The two Zhang et al. references disclose the coculture of bladder urothelial and smooth muscle cells on small intestinal submucosa; however, neither reference teaches, discloses or even suggests the use of bone marrow stromal cells, nor does either reference teach, disclose or suggest the differentiation of a multipotent cell (i.e., bone marrow stromal cell) into another

cell type (i.e., smooth muscle-like cell) while seeded on small intestinal submucosa. Thus, the two secondary references add nothing to the fact that the primary reference of Badylak et al. does not teach, disclose or even suggest the inventive concept recited in the pending claims.

In addition, Zhang et al. (*Journal of Urology*, 2000) was published in September 2000, and the effective filing date of the subject application is December 8, 2000. Since this publication is within one year of the effective filing date of the subject application and is a publication of the inventor's own work, it is not available as prior art under 35 U.S.C. 102/103. A Declaration under 37 C.F.R. 1.132 disqualifying this reference as prior art was filed in the parent application US Serial No. 10/013,270 on April 20, 2005, and a copy is attached hereto as Exhibit A. Therefore, Applicants respectfully submit that Zhang et al. (*Journal of Urology*, 2000) is not a proper reference under 35 U.S.C. 103(a).

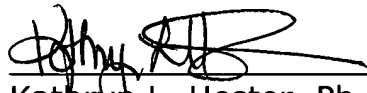
Applicants respectfully submit that pending claims 1, 6, 7, 10, 13, 24, 25, 44 and 45 are non-obvious over Badylak et al. in view of Zhang et al. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 103(a) rejections of the claims as now pending.

CONCLUSION

This was meant to be a complete response to the Office Action mailed May 10, 2005. Applicants respectfully submit that each and every rejection of the claims, as now pending, has been overcome. Further, Applicants respectfully submit that claims 1, 6, 7, 10, 13, 24, 25, 44 and 45, as now amended, are patentable over the art of record and are in a condition for allowance. Favorable action is respectfully solicited.

Should the Examiner have any questions regarding this Amendment, or the remarks contained herein, Applicants' agent would welcome the opportunity to discuss such matters with the Examiner.

Respectfully submitted,



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